44. The method of Claim 40, wherein the second solution having a selected pH has a pH of less than 7.

B1 concl.

45. The method of Claim 41, wherein the first solution of said aqueous medium has a pH of 5.0 and wherein said second solution added to the external liposome phase raises the pH of the external liposome phase to 7.4.--

REMARKS

Entry of the foregoing and reexamination and reconsideration of the above identified application are respectfully requested.

The Examiner, Dr. Kishore, is thanked for the courtesy of the interview conducted with the undersigned attorney on April 9, 1996. During that interview, the undersigned advised the Examiner that a new set of claims would be presented. More particularly, by this amendment, the claims have been rewritten to make more clear the method of the present invention. Support for these new claims may be found at the very least at pages 7-10 of the application.

Applicants would like to call the Examiner's attention to copending Application Serial No. 07/741,305, which is involved in Interference No. 103,469. Secrecy of the copending application under 35 U.S.C. §122 is maintained. The count of that interference corresponds precisely to Claim 1 of Forssen, U.S. Patent No. 4,946,683. That count is reproduced as follows:

> A method of preparing a phospholipid-entrapped cationic, lipophilic drug composition which comprises:
>
> (a) forming liposomes in an aqueous medium containing an acid which has at least one ionizable functional group, is of sufficient polarity to be highly soluble in water and exhibits a low permeability through the vesicle membranes to give an acidic liposome-containing aqueous medium in which the acid is present in the internal and external liposome phases, said liposome being prepared from hydroxyamino(lower)aliphatic-substituted phosphatidyl carboxylic acid diesters of a tri- or higher functional aliphatic polyol in which the ester moieties are derived from a saturated or ethylenically unsaturated aliphatic monocarboxylic acid having at least 14 carbon atoms,
>
> (b) adding to the thus-obtained acidic liposome-containing aqueous medium a cationic, lipophilic drug, and
>
> (c) then adding a base whose cations cannot pass through the liposomes' lipid bilayers to charge neutralize the acid anions in the external aqueous phase, thereby inducing the cationic, lipophilic drug to pass into the liposomes' internal aqueous phase.

It will be appreciated that the claims being added by the present Amendment are somewhat broader in scope than is the count of the interference. More particularly, the count of the pending interference requires that the pH gradient between the internal aqueous phase of the liposome and the external aqueous phase be established by forming liposomes in an aqueous medium containing an acid and then adding a base to the external phase. By contrast, Claim 27 added by the present Amendment requires only that a pH gradient exist between the external and internal phases. Such gradient could be created between an acid and a base as recited in the count of the interference. However,

such gradient could also be created between stronger and weaker acids or between stronger and weaker bases.

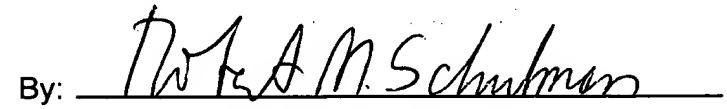
It was indicated during the interview that it may be necessary to suspend prosecution of the present application in view of the count of the pending interference. In this regard, reference was made to MPEP 2315.01 which mandates that the divisional of an application in interference should be "carried as far as possible." Thus, it was agreed that the claims would be examined for compliance, for example, with Section 112, first and second paragraphs. Nonetheless, because the present application "contains claims broad enough to dominate matter claimed in the application involved in the interference," suspension may be appropriate once all other issues have been resolved.

As indicated above, the newly added claims are believed to be fully supported by the original parent application. Furthermore, with the possible exception of the count in the pending interference, the newly added claims are believed to be completely free of the prior art. In this regard, it is noted that even though the claims added by the present Amendment are somewhat broader than those involved in the pending interference, the patentability issues are for the most part the same. More particularly, in both instances it is the establishment of a pH gradient to prepare a liposome vesicle-entrapped chemical species which is the patentable invention, not whether that gradient is established by acid/base (as set forth in the interference) or by more acidic/less acidic or more basic/less basic reagents. Thus, just as the method using an acid/base gradient was found to be

The Commissioner is hereby authorized to charge any fees under 37 C.F.R. §§1.116 and 1.117 that may be required by this paper, and to credit any overpayment, to Deposit Account No. 02-4800.

Respectfully submitted,

BURNS, DOANE, SWECKER & MATHIS, L.L.P.

By: 

Robert M. Schulman
Registration No. 31,196

Post Office Box 1404
Alexandria, Virginia 22313-1404
(703) 836-6620

Date: June 7, 1996